

E4 14. The method of claim 1, wherein the chimeric protein comprises Sup35 in which the N-terminal domain has been replaced by amino acids 1-42 of β -amyloid protein.

REMARKS

A. Status of Claims

The parent of this application was filed on December 8, 1998 with claims 1-36. It claims priority to U.S. Application Serial Number 60/069,168, filed on December 9, 1997, now abandoned, and U.S. Application Serial Number 60/084,824, filed on May 9, 1998, now abandoned. In subsequent prosecution, claims 2, 5, 6, and 21 were cancelled and claim 37 added.

The present application is a continuing application of the parent under 37 C.F.R § 1.53(d). In a Preliminary Amendment filed with the present application, claims 23-36 were cancelled, claims 1 and 4 were amended, and claims 38-40 were added. In the Office Action dated 10/24/00, claims 1, 3, 4, 7-20, 22, 37-40 were rejected; claims 38-40 were found to be directed to a nonelected invention and withdrawn from consideration. Herein, claims 1, 7, 12, and 14 are amended and claim 4 cancelled, without prejudice or disclaimer. Support for the amendments can be found in the Specification at least at page 5, line 27 to page 6, line 6; page 6, lines 17-21 and in the originally filed claims.

Thus, claims 1, 3, 7-20, 22, and 37-40 are pending and are the subject of this response. Attached as Appendix A is a copy of the claims with the amendments submitted herewith shown. Appendix B is a copy of the claims pending in this case after entry of the Amendment.

B. Claims 4 and 7-14 Are Enabled under 35 U.S.C. § 112, first paragraph

The Action rejects claims 4-14 under 35 U.S.C. § 112, first paragraph, as not providing enablement for a mammalian aggregate-prone amyloid protein wherein the protein is chimeric. It cites Lazar *et al.*, *Mol. Cell. Bio.* 8:1247-52, 1988, as recognizing that proteins are highly dependent upon sequence structure and that a single mutation of a protein can affect the biological activities of the molecule. Applicant respectfully traverses this rejection.

The claims were previously amended to clarify that the claimed methods involve a “yeast cell that expresses an aggregate-prone amyloid protein comprising a mammalian aggregate-prone amyloid protein.” The amendment reflects that an “aggregate-prone amyloid protein” contains amino acid sequence of a “mammalian aggregate-prone amyloid protein,” such as all or part of the β -amyloid protein. *See* Specification at page 5, line 26-page 6, line 6. The term “mammalian” simply refers to the protein sequence source, which is a mammal. The protein could comprise amino acid sequences from two different mammalian sources, which would render it chimeric, according to the disclosure. *See e.g.*, Specification page 5, lns 28-29 (“By ‘chimeric protein’ it is meant that the protein comprises polypeptides that do not naturally occur together in a single protein unit.”).

The Action contends that the specification defines no mammalian chimeras. It also alleges that it would take undue trials and errors to practice the claimed invention given the quantity of necessary experimentation, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance and the breadth of the claims.

In contrast to the statements in the Action, the specification does disclose mammalian chimeras. The specification describes mammalian aggregate-prone amyloid proteins as including PrP and β -amyloid polypeptide. *See* Specification page 5, lns. 22-24. As mentioned

above, it also defines a “chimeric protein.” See Specification page 5, lns. 28-29. Moreover, the specification also describes examples of chimeric proteins that comprise “at least an aggregate forming domain of a mammalian amyloid polypeptide, such as at least amino acids 1-42 of the β -amyloid protein or at least the aggregate forming domain of PrP.” Specification page 6, lns 2-4. The disclosure further mentions that the methods of the invention may employ a “protein comprising the aggregate forming domain of the etiological agent of a particular disease in the yeast system to identify therapeutic compounds for that disease,” and it lists some amyloidogenic diseases in animals, such as Alzheimer’s disease, scrapie, and spongiform encephalopathy. Specification page 7, lns 20-24. The specification states, “Therefore, in determining therapeutic compounds for Alzheimer’s disease, one would use a yeast system comprising at least amino acids 1-42 of the β -amyloid protein.” Specification page 7, lns 24-26. It also similarly states that the aggregate-forming domain of PrP may be utilized in the methods of the invention. Moreover, a specific example of a chimeric protein comprising the β -amyloid peptide (1-42) and the Sup35 C terminal domain is mentioned as being particularly useful in screening for the [PSI⁺] phenotype. See Specification page 13, lns. 22-25. Thus, the disclosure does define mammalian chimeras.

As for the Action’s contention that it would require undue trials and errors to practice the claimed invention, Applicant points to the state of the art at the time the application was filed coupled with the disclosure of the application. The reference of Hughes *et al.*, which is cited by the Action, involves fusion proteins. Fusion proteins are chimeric proteins, and the Hughes *et al.* paper describes a fusion protein that contains a portion of the β -amyloid peptide. It shows how fusion proteins are made and that they are functional. This paper unequivocally supports the contention that one of skill in the art could make and use chimeric proteins comprising a

mammalian aggregate-prone amyloid protein at the time the present patent application was filed, and that the invention can be practiced without undue experimentation.

“The specification must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” MPEP 2164.08 (citing *In re Wright*, 999 F.2d 1557, 1561, 27 U.S.P.Q. 1510, 1513 (Fed. Cir. 1993)). The methods of making such a chimera and employing it in the described methods would not be undue because the specification teaches how to use peptide regions that would be comprised in a chimeric protein and because recombinant techniques for making chimeras and administering them to a yeast cell were well-known at the time the application was filed, as is evidenced by the Hughes *et al.* paper. “The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available in the public.” MPEP 2164.05(a) (citing *inter alia*, *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q. 2d 1331, 1332 (Fed. Cir. 1991)). Thus, the applicant need not disclose methods for constructing such a chimeric protein because the application discusses various combination and the recombinant technology was readily accessible to the skilled artisan.

Furthermore, Applicant respectfully notes that “it is incumbent upon the Patent Office...to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.” MPEP 2164.05 (quoting *In re Marzocchi*, 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (CCPA 1971)). The specification explicitly says that “yeast expressing a chimeric protein comprising the β -amyloid peptide (1-42) and the Sup35 C-terminal domain have a [PSI⁺] phenotype that leads to cell death.” Specification page 13 lns. 23-25. Applicant requests an explanation as to why it doubts this statement and to provide a reference

that indicates the claimed invention would not work. The citation of Lazaro *et al.*, a reference that is more than 10 years-old, is irrelevant to the enablement of the present invention because it concerns a protein (TGF α) completely unrelated to the proteins described in the application and it involves mutation of a protein in a region highly conserved which is not at all similar to the type of domain swapping involved in generating the chimeric proteins of the present application. This reference has no specific applicability to the claimed invention. Even if it did, as discussed above, there is information that indicates how to make and use a “chimeric aggregate-prone amyloid protein comprising a mammalian aggregate-prone amyloid peptide.”

Thus, Applicant contends that the specification does enable claims 4-14 and that the arguments provided by the Examiner do not support a *prima facie* case to the contrary. Accordingly, Applicant respectfully requests the withdrawal of this rejection.

C. Claims 4 and 7-14 Are Definite under 35 U.S.C. § 112, second paragraph

Claims 4 and 7-14 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that the applicant regards as the invention. Two different arguments are asserted. First, the Action contends that it is contradictory that a mammalian protein is a chimeric protein (a protein having foreign sequences). Second, it alleges that the recitation “an aggregate forming domain” is indefinite because the skilled artisan has no guidance by which to determine that portion of a chimeric protein which forms an “aggregate forming domain.” Applicant respectfully traverses both grounds.

Applicant points out that claim 1 (as amended) recites an “aggregate-prone amyloid protein” not a “*mammalian* aggregate-prone amyloid protein.” It is not contradictory that an

aggregate-prone amyloid protein comprising a “mammalian aggregate-prone amyloid peptide” is a chimeric protein. As such, claim 1 and claims depending from it are not indefinite.

The standard for definiteness of a claim is whether a person of skill in the art can determine the scope of the invention based on the language of the claims with “a reasonable degree of certainty.” MPEP 2173.02 (citing *In re Wiggins*, 488 F.2d 538, 179 U.S.P.Q. 421 (C.C.P.A. 1973)). Claims 7 and 12 recite a chimeric protein that comprises at least an “aggregate forming domain” of “a mammalian aggregate-prone amyloid protein” or “PrP or β -amyloid.” Based on portions of the Specification, for example page 6, lines 2-5 and page 14, lines 1-3, a person of skill in the art, coupled with knowledge of the art, that an “aggregate forming domain” refers to the amino acids of an aggregate-prone amyloid protein that are involved in aggregation. The disclosure in the Specification that amino acids 1-42 of the β -amyloid protein and amino acids at the N-terminal domain of Sup35 satisfy the limitation of an “aggregate forming domain” eliminates any indefiniteness of what constitutes an “aggregate forming domain.”

That one of skill in the art may have to figure out what portions of an aggregate-prone amyloid protein constitute an aggregate forming domain does not render the claim indefinite. As mentioned above, the MPEP simply requires that a person of skill in the art be able to determine the scope of the claim. In this case, the claims employ a phrase that can be easily understood, the Specification employs that phrase consistent with its use in the claims, and furthermore, the Specification identifies ways of determining whether a protein aggregates, for example, at page 13, lines 2-3. Thus, not only is the scope of the claim fully ascertainable to a person of ordinary skill in the art, but that person would be able to practice what he understood to be the invention.

Accordingly, the claim fulfills 35 U.S.C. § 112, and the rejection is respectfully requested to be withdrawn.

D. Claims 3 and 12-14 Are Definite under 35 U.S.C. § 112, second paragraph

The Action rejects claims 3 and 12-14 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that the applicant regards as the invention. The term “PrP or β -amyloid polypeptide” is alleged to be indefinite. The Action argues that the skilled artisan recognizes a multitude of forms of prion proteins and the specification contains reference to a PrP^c and PrP^{sc}. It also contends that a “name by itself does not structurally define a protein without specific references,” and it cites Wickner, *Science* 264: 566-569, 1994, for teaching that the skilled artisan recognizes that prion proteins have divergent structures and share characteristics as specified. The previous Office Action argued that it was not clear whether “PrP” refers to a prion protein defined by the ability to aggregate or whether “PrP” and “ β -amyloid” intend to convey a certain structure. It also argues that metes and bounds of “aggregate” are unclear and that the Applicant’s contemplation of amyloid proteins appears to contradict the structural limitations recognized in the art. Applicant respectfully traverses. Applicant reiterates arguments made in the Response to Final Office Action dated February 1, 2000 as the current Action seems to indicate that the arguments made in this document were considered in rendering these arguments.

“Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

- (A) The content of the particular application disclosure;
- (B) The teachings of the prior art; and
- (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.” MPEP 2173.02.

Applicant contends that the terms “PrP,” “ β -amyloid polypeptide,” and “mammalian aggregate-prone amyloid protein” are all clear and definite and that one of skill in the art would fully understand the metes and bounds of the claim. Applicant also argues that a person possessing ordinary skill in the art would understand that “PrP” refers to **the** mammalian prion protein and that “ β -amyloid polypeptide” refers to a particular mammalian amyloid-forming protein, both of which have been the subject of numerous papers, none of which discloses any uncertainty in the identity of these polypeptides. PrP refers to a specific mammalian protein encoded by a specific gene, whose sequence depends on the mammal from which it was derived and on polymorphic differences. *See e.g.*, Genbank Accession Nos. D26151 and AF163764 (encoding part of exon 3 of the bovine PrP and other parts of the bovine PrP gene, respectively) and U29185 (encoding entire human PrP gene). The specification makes reference to PrP or β -amyloid polypeptide throughout its contents, for example, at page 14, line 29 to page 15, line 4; page 15, lines 11-20; page 15, line 26 to page 16, line 2; page 16, lines 26-29; page 22, lines 17-21; and page 23, lines 28-30. These references throughout the disclosure are entirely consistent with one another and the usage of the terms “PrP” and “ β -amyloid polypeptide” in the art.

Furthermore, the disclosure is unequivocally clear that “[a]ggregate-prone amyloid proteins include...mammalian proteins, such as Prp and β -amyloid polypeptide.” Specification p. 5, lns 22-24. Prp and β -amyloid polypeptide are not merely proteins that can aggregate; instead, the specification teaches they are amyloid proteins, which indicates they are capable of forming amyloid or amyloid-like deposits that are generally insoluble fibrillary material. *See* Specification p. 5, lns 18-20. Thus, aggregation is *necessary* but not *sufficient* to qualify a protein as an aggregate-prone amyloid protein. *See* Patino *et al.*, *Science* 273:622-626, 624

(1996) (showing in Fig. 3C a protein that aggregates (GFP-t) but would not qualify as a prion since it is “not inherited”). As PrP is an example of an aggregate-prone amyloid protein, a protein that aggregates must also be able to form amyloid to be a PrP. Finally, PrP is a term that refers to a particle mammalian gene that is responsible for mammalian encephalopathy, for example, in bovine, feline, a mink, deer, elk, a mouse, a hamster, a monkey, or a human. See Specification p. 7, line 27 to page 8, line 2.

The state of the art at the time the application was filed reflects the understanding of a skilled artisan with respect to amyloid proteins, particularly that amyloid proteins form amyloids, which is a distinct structure, not merely an aggregation of protein. In Serpell *et al.* (attached as Appendix B), molecular properties considered to be diagnostic of an “amyloid” were said to include: 1) the appearance of uniform fibrils under an electron microscope; 2) the ability to be stained with Congo Red; and 3) an x-ray diffraction pattern indicative of a cross- β structure. Serpell *et al.* at 871-72. Thus, it is clear that not any mammalian protein that aggregates is an “aggregate-prone amyloid protein” that encompasses PrP, the mammalian prion protein, and β -amyloid polypeptide. As such, the claim interpretation that would be given to these terms by one possessing the ordinary level of skill in the pertinent art at the time the invention was made is an interpretation that is wholly consistent with both the specification and the art.

The Action does not cite any prior art that indicates a meaning different for either “PrP” or β -amyloid polypeptide” than is provided by the specification. Moreover, Applicant wishes to clarify a statement in the response to the previous Office Action. Applicant stated, “The claims are not directed to ‘prion proteins’ as the Action seems to suggest....” Applicant instead intended to argue that the rejected claims are not directed to generic prion protein, *i.e.*, any prion proteins, but instead are limited to a particular type of mammalian prion protein, PrP, or to a β -

amyloid polypeptide, which is why Wickner's teaching of divergent *yeast* prion proteins is irrelevant. The studies of Wickner involved yeast polypeptides. This provided the basis for his statement that his findings suggest that a broader definition of a prion may "include any protein that indefinitely propagates an altered form of itself...and is transmissible." Wickner at 568. However, this statement was in the context of yeast proteins. It indicates that one of skill in the art would ordinarily not define a "prion" that broadly, much less a "mammalian prion protein" or "PrP." Furthermore, Wickner expressly states, "Prion proteins have been described in many vertebrates. These proteins are all *highly homologous with each other....*" *Id.* (emphasis added). This statement applies to mammalian prion proteins, which are the subject matter of the claims. Therefore, Wickner does not stand for the proposition that the prion proteins of the claimed invention have a divergent structure, and it does not support the Action's contention that one of skill in the art would not understand what PrP is.

Furthermore, Applicant does not understand the argument in the Action about an "aggregate-prone amyloid protein." As the Specification makes clear, as discussed above, such a protein is capable of aggregation under physiological conditions **and** forming amyloid or amyloid-like deposit. There is nothing inconsistent in this statement and there is no uncertainty about what the term means.

Accordingly, Applicant contends that the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity and respectfully urge that the rejection of claims 3 and 12-14 for indefiniteness be withdrawn.

E. Claims 1, 3-4, 7, 12-13, and 17-18 Are Not Anticipated by Hughes *et al.*

The Action rejects claims 1, 3-4, 7, 12-13, and 17-18 under 35 U.S.C. § 102 (b) as being anticipated by Hughes *et al.*, PNAS, 93:2065-70, 1996 (“Hughes *et al.*”). Claims 8-11, 14-16, 19, 20, and 22 are rejected as depending from a rejected claim. The Action contends that Hughes *et al.* clearly measures the interaction of A β peptide aggregates as evidenced by Figure 1, which anticipates the invention because it does not exclude the interaction of A β monomers. Applicant respectfully traverses.

The Action argues that the Hughes *et al.* reference discloses a method that is the same as the claimed invention. It cites Figure 1 as showing that the two hybrid system measures the interaction of A β peptides. However, Applicant disputes that Hughes *et al.* teaches the claimed method because the method it discloses simply cannot be employed in the way the claimed invention requires by the recited steps. The Hughes *et al.* reference describes a typical use of the yeast two-hybrid system. Applicant once again points out that Figure 1 precisely shows that the system can evaluate only the ability of monomers to associate. The steps of the claimed invention specifically evaluate “aggregated amyloid formation” as the assay is set up under conditions effective to allow “aggregated amyloid formation.” The two-hybrid system of Hughes *et al.*, on the other hand, relies on the ability of two molecules to interact in the nucleus to promote transcription of a reporter gene, which is then assayed. The Hughes *et al.* reference states, “The yeast system described in this paper offers an opportunity to study the interaction of monomeric A β peptides....This system may therefore provide an opportunity to freeze-frame the monomer-monomer interaction.” Hughes *et al.* p. 2070. Figure 1 also confirms this in its description: “The system therefore provides an opportunity to examine interaction between two monomeric A β molecules....” The specification states that “amyloid or amyloid like deposits

are generally insoluble fibrillary material.” Page 5, lines 19-20. This indicates not only that the method of Hughes *et al.* is not performed under conditions to promote “aggregated amyloid formation,” which is a limitation recited by the claims, but also that it *would not be* performed under such conditions because such aggregation of the monomers would prevent transcription—the very event being assayed—from occurring at all.

Moreover, the Hughes *et al.* reference makes it clear that the authors are not investigating aggregation, but the interaction of monomers. In the opening paragraphs of the article, the rationale for the studies in the article are described:

Kinetic studies on A β aggregation have demonstrated that amyloid formation is a nucleation-dependent phenomenon, and that lag time precedes aggregation, the length of which may depend on protein concentration. The nucleation even may therefore be the rate-determining step of *in vivo* amyloidosis...Interaction between two monomers, a thermodynamically unfavorable intermolecular interaction, may be a critical step in nucleation.

Hughes, page 2065, col. 2 (citations omitted). Thus, it is clear that monomer formation is hypothesized as part of a nucleation event that *precedes aggregation*. This is evidence that a person of skill in the art, reading the specification and claim language—particularly “under conditions effective to allow aggregated amyloid formation”—would not interpret the claims as encompassing monomer interactions, and thus as reading on the Hughes *et al.* reference.

Also, the Hughes reference admits that the system it uses “may not be relevant to fibril formation,” which is evidence of the reference’s inapplicability to the claimed methods that specifically concern aggregated amyloid formations. Hughes *et al.* p. 2070.

Furthermore, nowhere in the reference is there a suggestion that the assay be performed under conditions to promote aggregated amyloid formation, which is not surprising given that the

assay was not intended to evaluate amyloid formation. The steps of the rejected claims recite: “(a) contacting a yeast cell that expresses a mammalian aggregate-prone amyloid protein with said candidate substance under conditions effective to allow aggregated amyloid formation; and (b) determining the ability of said candidate substance to inhibit the aggregation of the mammalian aggregate-prone amyloid protein.” Patent law requires that “a rejection for anticipation under section 102 requires that each and every limitation of the claimed invention be disclosed in a single prior art reference.” *In re Paulsen*, 30 F.3d 1475, 31 U.S.P.Q. 2d 1671 (Fed. Cir. 1994). The limitation that steps of the assay be performed “under conditions effective to allow aggregated amyloid formation” is conspicuously absent from the cited reference, but as mentioned above, not surprising given the objective of the methodology in Hughes *et al.* The yeast two-hybrid system is a widely used, well understood assay that relies on the ability of two polypeptides to bind DNA in a specific (as opposed to non-specific) manner and to associate in a stereo-specific way with proteins that form part of the host cell’s transcriptional machinery. This assay is critically dependent on the ability of the polypeptides involved in the assay to reach the nucleus so they can specifically interact with one another to transcribe the reporter gene being assayed. See Phizicky and Fields, *Microbiol. Rev.* 59:94-123, 106 (1995) (“The two-hybrid system is limited to proteins that can be localized to the nucleus, which may prevents its use with certain extracellular proteins.”) (Appendix C). In the assays of the present invention, aggregation prevents the polypeptides from reaching the nucleus. In the context of the Hughes *et al.* reference, aggregation of a mammalian aggregate-prone amyloid proteins causes them to be insoluble such that the A β monomers in the two-hybrid system would be unable to associate in the nucleus, and they would be unavailable to promote transcription. Therefore, the yeast-two

hybrid system is simply inoperable for the intended purpose of the assay if practiced according to the limitations of the claimed invention.

Thus, Applicant contends that the method of Hughes *et al.* is not operable with respect to the claimed method, according to the Hughes *et al.* disclosure and to the application's disclosure because monomer association is not within the scope of the phrase "aggregated amyloid formation" based on the specification of the present application. As a limitation of the claim is not met by the cited reference, a rejection based on anticipation is improper, and Applicant respectfully requests its withdrawal.

F. Claims 4-14 Are Not Anticipated by the Cited Art

The Action rejects claims 4-14 as anticipated under 35 U.S.C. § 102 (b) by Wickner *et al.*, Chernoff *et al.*, Paushkin *et al.*, and Patino *et al.* It alleges that even though the claims recite a mammalian aggregate-prone amyloid protein, the claimed chimeric protein is no different than the yeast proteins in the references since amyloid and prion protein share sequences in common. Applicant respectfully traverses and reiterates arguments made in the Response to the Final Office Action, as they seem not to have been previously considered.

Every recited element of a claim must be disclosed by a reference for it to anticipate a claim. See *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). While it may be true that a chimeric protein of the claimed invention can contain yeast prion sequences disclosed by Wickner *et al.*, Chernoff *et al.*, Paushkin *et al.*, and Patino *et al.*, it is not the case that these references disclose a chimeric aggregate-prone protein that contains mammalian sequence. The Action has presented no sound basis for asserting that references that describe yeast prions necessarily disclose protein sequences from *mammalian* aggregate-prone proteins. If the grounds for this rejection are to be

maintained, the Examiner is requested to provide evidence in the form of a reference or affidavit that supports the contention that yeast prion sequences are so similar to mammalian aggregate prone proteins that they are virtually identical. *See* MPEP § 2144.03.

In fact, the specification teaches that PrP, a mammalian prion protein, and Sup 35, a yeast protein that forms aggregates, have **no** sequence identity and are functionally unrelated. Specification page 34, lines 6-8. Sup35 is the subject matter of the Chernoff *et al.*, Patino *et al.*, and Paushkin *et al.* papers and is closely related to [URE3], the subject of the Wickner *et al.* reference. Thus, the statement in the specification calls into question the Action's assertion that the sequences of the cited art and the subject matter of the invention are similar.

Applicant contends that a proper *prima facie* case of anticipation has not been made because identity is clearly lacking. Accordingly, Applicant respectfully requests this rejection be withdrawn.

G. Claims 1, 3, 15, 17-19, and 37 Are Not Anticipated by Cordell *et al.*

The Action rejects claims 1, 3, 15, 17-19, and 37 under 35 U.S.C. § 102 (b) as anticipated by Cordell *et al.* (Cordell). Cordell is said to teach assays and reagents for amyloid deposition including the identification of agents that inhibit amyloid formation. The Action also contends that the amyloid products produced may be expressed in yeast and include beta amyloid 1-42 and preamyloid precursors. Applicant respectfully traverses this rejection.

As discussed above, anticipation of a claim requires that every element be taught by a cited reference. Cordell does not teach a “chimeric aggregate-prone amyloid protein” anywhere in the disclosure, which is required by the claims, as amended. There is also no suggestion of a chimeric protein, much less that the reference should be combined with another reference. For

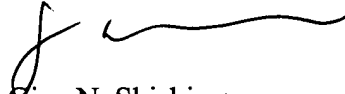
example, Cordell says, “In one embodiment of the invention, a CHO cell line transformed with a beta-actin vector comprising the DNA encoding the A42 or A99 amyloid protein....” Cordell at page 16, lines 26-28. No mention is made here, or anywhere else about fusing an amyloid protein with another protein.

The cited reference does not teach each element of the claimed invention. As a matter of law, it does not anticipate the claimed invention. Applicant respectfully requests this rejection be withdrawn.

H. Conclusion

Applicant believes that the present document is a full and complete response to the referenced Official Action. In conclusion, Applicant submits that, in light of the foregoing remarks, the present case is in condition for allowance and such favorable Action is respectfully requested. Should the Examiner have any further questions or comments, or believe that certain clarifications might more readily progress the present application to issuance, a telephone call to the undersigned Applicant’s representative at (512) 536-3081 is earnestly solicited.

Respectfully submitted,



Gina N. Shishima
Reg. No. 45,104
Attorney for Applicant

FULBRIGHT & JAWORSKI
600 Congress Avenue
Suite 1900
Austin, TX 78701
Telephone: (512) 536-3081

Date: March 26, 2001